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TRANSVAGINAL SLING USING ACELLULAR HUMAN DERMAL ALLOGRAFT: SAFETY AND EFFICACY IN 253 PATIENTS

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ABSTRACT

Purpose: We evaluated the safety and efficacy of using human dermal allograft material for transvaginal slings to treat female stress urinary incontinence (SUI).

Materials and Methods: We present a prospective series of 253 patients with SUI treated with a transvaginal sling using a Repliform cadaveric human dermal allograft (LifeCell Corp., The Woodlands, Texas) and a bone anchor fixation kit. Clinical history, urogynecologic examination and videourodynamics were performed preoperatively. Results were assessed by a third party through validated quality of life questionnaires (Incontinence Impact Questionnaire and Urogenital Distress Inventory), overall impression and percent of improvement as perceived by the patients, and pad use. Scheduled followup examination were performed to rule out erosion, infection, obstruction, pain or recurrent incontinence.

Results: Complete followup was available on 234 of 253 patients. Average followup was 18 months. Of the patients 78% were cured or improved according to the questionnaires. The average improvement was 80%. At 18 months of followup incontinence average distress and scores decreased 10 and 7 points, respectively. Complications were de novo urgency in 5% of cases, recurrent SUI in 15% with no cases of persistent SUI, retention in 2% and slow vaginal wall healing in 1.7%. Of 156 patients 51 (22%) had persistent urgency. There were no cases of vaginal or urethral erosion, osteitis pubis or osteomyelitis.

Conclusions: Our data indicate that use of human dermal allograft for transvaginal slings is associated with low complication rates and favorable outcomes at an average of 18 months of followup.

KEY WORDS: urethra; transplantation, homologous; urinary incontinence, stress; vagina

Sling surgery has evolved in many ways during the last decade. The original indications for the sling procedure were incontinence associated with poor urethral sphincter function[1] and the original purpose of the sling procedure was to increase urethral resistance by elevating the urethra toward the pubic bone. The procedure was effective for restoring continence but at the cost of increased urinary obstruction and urgency symptoms. Attempts to limit obstructive voiding problems while treating intrinsic sphincter deficiency included tying attachment sutures loosely, the development of injectable materials,[2] the use of artificial urinary sphincter[3] and more recent tension-free techniques, such as a TVT (tension-free vaginal tape), SPARC (suprapubic arc restoration of continence (American Medical Systems, Minneapolis, Minnesota) or transobturator tape procedure. Tension-free techniques move the sling position to mid urethra and extend indications to patients with hypermobility. Sling attachment varies from rectus fascial fixation, various bone anchors and the newer tension-free self-anchoring sling. Sling material varies from anterior vaginal wall, autologous or homologous fascia, cadaveric dermal graft to xenograft (intestinal submucosa or porcine skin) and a plethora of synthetic materials,[4–7] but the ideal material remains debatable. We present our prospective series of 253 patients treated with a transvaginal sling using Repliform cadaveric human dermal allograft and a bone anchor fixation kit (Boston Scientific Corp., Watertown, Massachusetts) to evaluate the safety and efficacy of this material.

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MATERIAL AND METHODS

From June 1998 to April 2003, 253 patients with stress urinary incontinence (SUI) who had received a Repliform transvaginal sling were evaluated prospectively. All patients completed validated quality of life questionnaires, namely the Urogenital Distress Inventory (UDI) and Incontinence Impact Questionnaire (IIQ) (see Appendix)[8] before surgery and postoperatively at each visit. In addition to a detailed history, complete physical examination and a 24-hour voiding diary, all patients underwent videourodynamics. The number of daily incontinent pads used was noted before and after surgery.

Operative technique. Two surgeons performed the transvaginal sling procedures using Repliform. All patients received preoperative antibiotics (cephazolin or fluoroquinolone). Patients were placed in the lithotomy position after satisfactory general or epidural anesthesia was established. A 20Fr Foley catheter was inserted and the labia were sutured laterally for better exposure. After hydrodissection of the anterior vaginal wall with saline a midline anterior incision was made. The vaginal mucosa was dissected from the periurethral and perivesical fascia on each side and the retropubic space was entered and digitally dissected.

The sling was rehydrated in normal saline for 3 to 5 minutes. The 2×4 cm graft was used most often. Using permanent polypropylene sutures the graft was anchored to the pubic bone using the bone anchor kit.[9] Graft edges were fixed to the proximal urethra using 4, 3-zero polyglactin sutures. The distal edge of the graft was sutured at the mid urethra and the proximal edge was sutured at the bladder neck. Following sling placement the polypropylene sutures were

tied against a 20Fr cystoscope placed in the urethra at a 45-degree angle to the horizontal operative table. Cystoscopy was performed to rule out bladder or ureteral injuries after indigo carmine was administered. Concomitant cystocele, rectocele, enterocele or sacrospinal suspension procedures were then performed. If vaginal hysterectomy were required, a gynecologist performed it before the sling. Intraoperative and in hospital complications, estimated blood loss and inpatient days were noted. All patients received antibiotics and catheter drainage for 3 to 7 days depending on the extent of surgery. Patients were encouraged to continue behavioral technique and Kegel exercises.

Patient characteristics (table 1). Between June 1998 and April 2003, 253 patients underwent a transvaginal sling procedure with Repliform, bone anchors and concomitant vaginal reconstructive procedures. Complete followup was available on 234 patients. Average patient followup was 18 months (range 6 to 54), including 100 patients (42%) with a followup lower and 134 (58%) with a followup higher than 12 months. Average patient age was 58.3 years. Average parity was 3. Of 234 patients 133 (57%) had undergone previous pelvic procedures. This group had undergone a total number of 241 pelvic procedures, of which 100 (42%) were antiincontinence procedures and 80 (33%) were retropubic (table 1). All except 10 patients had stress urinary incontinence by history and confirmed by videourodynamic studies. The average cough leak point pressure was 65.7 cm H_2O (range 9 to 210) and the average Valsalva leak point pressure was 64.4 cm H_2O (range 9 to 183). The urodynamic classification of SUI using a Valsalva leak point pressure of 60 cm H_2O as the cutoff point revealed that 112 patients had type III SUI, while 156 (61.6%) had a history of urgency or urge incontinence preoperatively, 79 (35.2%) had preoperative detrusor instability and 182 (77%) underwent a total of 302 concomitant procedures, including hysterectomy, cystocele, rectocele and enterocele repair, sacrospinous suspension and urethrolysis (table 1). Of the 234 patients 211 (90.1%) used pads before surgery (average 3 daily).

Postoperative followup. Routine followup consisted of visits at 3 to 7 days (voiding trial), 1 and 3 months, and every 6 months thereafter. Patients were asked by a third party to complete validated quality of life questionnaires that addressed self-reported continence and voiding status. Questions regarding pad use, dyspareunia, prolapse, improvement or worsening of incontinence, urgency and obstructive symptoms were asked. In addition, at 1 and 2 years patients received mailed questionnaires to complete privately at home. Overall patient satisfaction for stress and urge incontinence was assessed by questions 2 and 3 on the UDI questionnaire. The questions had a 4-point scale of severity, including 0—dry (cured), 1—slight leakage (improved), 2—moderate leakage (failure) and 3—severe leakage (failure). Early and late postoperative complications were recorded.

RESULTS

Intraoperative complications (table 2). Intraoperative complications were 5 small bladder perforations (2.1%) and 2 small bowel perforations during enterocele repair. All complications were recognized intraoperatively and repaired immediately without sequelae.

Early complications (table 2). Early complications were perioperative bleeding in 3 patients, while 2 with hysterectomy required transfusions. Urinary retention requiring catheterization for 7 to 10 days occurred in 20 patients (8.5%), while the average number of days of postoperative catheter drainage was 4 in all patients. The 5 patients with bladder perforation were in this group and they underwent catheter drainage for 10 to 15 days. One perirectal abscess due to spontaneous defecation during surgery developed in a patient with a transvaginal sling, anterior and posterior repair, vaginal hysterectomy and sacrospinous suspension. Drainage at the bedside was successful. Remarkably the Repliform site used for the sling and anterior repair healed normally. There was 1 postoperative cerebrovascular accident within 30 days of surgery without permanent deficit.

Late complications (table 2). Late complications were transient dyspareunia in 20 cases (8.5%), of which 4 were successfully treated with removal of the ends of polypropylene sutures protruding in the vaginal wall. At 6 months postoperatively the remaining patients denied pain during intercourse. A total of 11 patients (6%) complained of postoperative pain (suprapubic in 5, vaginal in 5 and sciatica-type in 1). Most complaints ceased in 3 months and at 6 months all patients denied pain. Two patients (0.8%) complained of new constipation during 2 months, which gradually cleared. Five of the 20 patients (2.1%) requiring prolonged catheterization eventually complained of obstructive urinary symptoms, including 2 with neurogenic bladder and 1 with poor bladder sensation who occasionally used intermittent self-catheterization. Symptoms cleared in all patients except those with neurogenic bladder. There were 13 patients with new urgency (5.5%) and all used anticholinergics at last followup. Of 156 patients with preoperative urgency 51 (22%) had persistent urgency after the procedure. In 4 patients (1.7%) there was slow healing of the anterior vaginal wall over small areas of Repliform associated with vaginal infection, which was managed conservatively by antibiotic cream. Complete healing occurred within 8 weeks.

Outcomes. To evaluate outcomes as completely as possible certain parameters were completed, namely preoperative and postoperative IIQ and UDI scores (see Appendix), overall patient impression of results (dry or cured, slight or improved leakage, moderate leakage or failure, severe leakage or failure) for stress and urge incontinence, percent of improvement and pad use after surgery. Pad weight was not measured. The average recorded score on the IIQ questionnaire (maximum score 21) was 13.7 before surgery, 2.7 at 9 months

TABLE 1. *Previous surgery and concomitant procedures*

Procedures	No. Pts (%)	Type
Previous:	241	
Bulking agents	40 (17)	18 D, 22 C, # 2.15
Hysterectomy	105 (44)	45 VH, 60 AH
Prolapse repair	36 (14)	16 AR, 3 PR, 17 BOTH
Sling + suspension	60 (25)	13 PVS, 44 AS, 3 BOTH
Concomitant:	302	
Anterior repair	101 (13)	Repliform in 81
Posterior repair	3 (1)	Repliform in 2
Anterior + posterior repair	79 (26)	Repliform in 40
Sacrospinous suspension	59 (19)	Bilat in 38, rt in 20, lt in 1
Transvaginal hysterectomy	22 (7)	—
Enterocele repair	18 (6)	—
Urethrolysis	13 (4)	—
Uterosuspension	7 (2)	—

TABLE 2. *Intraoperative, early and late complications*

Complication	No. Pts (%)	Comment
Intraop:	234	
Bladder injury	5 (2.1)	—
Bowel injury	2 (0.9)	—
Early:	234	
Periop bleeding	3 (1.3)	After hysterectomy
Periop retention	20 (8.5)	Catheter for 7–10 days
Periop infection	1 (0.8)	Perirectal abscess
Periop vascular accident	1 (0.8)	Stroke
Late:	234	
Dyspareunia	20 (8.5)	Transient
Pain	11 (4.7)	Suprapubic in 5, vaginal in 5, sciatica type in 1
Constipation	2 (0.9)	
Obstructive symptoms	5 (2.1)	Neurogenic bladder in 2
New urgency	13 (5.5)	—
Slow vaginal wall healing	4 (1.7)	Vaginal infection

of followup and 3.5 at 18 months (fig. 1). The average UDI score (maximum score 18) was 11.6 before surgery, 3.1 at 9 months of followup and 4.3 at 18 months (fig. 2).

Figures 3 and 4 list overall patient impressions of results of surgery at a mean 18-month followup for stress and urge incontinence. The average percent improvement at 9 months was 85% and at 18 months it was 80%. Prior to surgery 90% of patients used an average of 3 pads daily. At 9 and 18 months after surgery pad use had decreased to 0.5 and 0.8 pads daily, respectively. The Table 3 lists the results of type II vs III SUI.

DISCUSSION

It appears that hypermobility of the bladder neck and a weak proximal complex are present in most women with stress incontinence and continence is probably achieved by supporting these 2 structures by creating a stable layer against which the urethra is compressed during stress.[10] This explains the current trend toward sling procedures throughout the world. While the pubovaginal sling has become the prominent surgical treatment for SUI, the ideal sling material remains debatable. Desirable qualities of sling materials are availability, durability, affordability, lack of immune response, resistance to infection and no potential for disease transmission. Autologous fascia offers biocompatibility and durability. Nevertheless, a second operative field is necessary with an attendant increase in postoperative pain and infection risk. Various cadaveric allograft fascia avoid the morbidity present with autologous fascia but some defects have been attributed to this material. Long-term successful treatment is questionable. Fitzgerald et al reported greater than 20% material failure.[11] Secondary vaginal erosion of cadaveric fascia lata used for abdominal sacrocolpopexy and suburethral sling procedures was reported in 25% of patients by Kammerer-Doak et al.[12]

The advantages of synthetic materials over autologous grafts for the surgical treatment of stress urinary incontinence are the avoidance of an additional incision to harvest fascia lata or rectus muscle fascia, a decrease in operative time, consistent material strength, high cure rates and decreased postoperative pain.[13] While cure rates and durability seem promising, several serious complications are concerning. Synthetic grafts are associated with a risk of rejection or erosion, most commonly into the vagina. The average reported erosion rate of synthetic grafts used for abdominal sacrocolpopexy is 2.7% and for suburethral slings it is 7.3% (range 3% to 34%).[14] Polytetrafluoroethylene slings have erosion and infection rates as high as 23%.[15] The ProteGen sling (Boston Scientific, Watertown, Massachusetts) was associated with infection or erosion and it was voluntarily recalled.[16] More recently, polypropylene material has been used in sling procedures, such as TVT and transvaginal obturator tape.[17] While short-term followup studies show high success with a low complication rate, several complications not fully reported in the literature have been identified. A search through the Food and Drug Administration adverse product reporting website (www.fda.gov/cdrh) revealed notable complications of the TVT procedure, including erosion, retention, bladder perforation, and major complications of vascular and bowel injuries, sepsis and rarely death. While these complications are probably not material related, caution is necessary in the use of TVT.

Repliform acellular human dermal allograft consists of

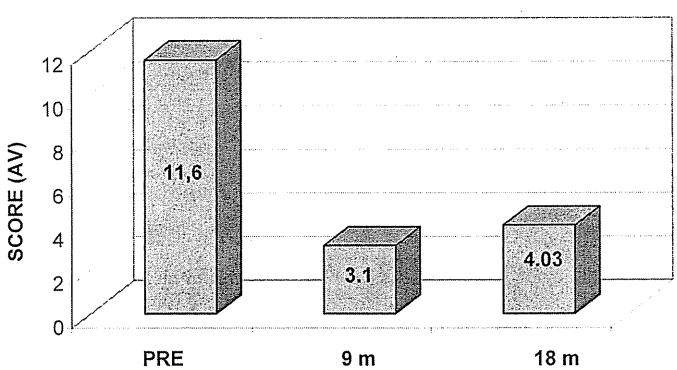

FIG. 1. IIQ results. *Av*, average. *PRE*, preoperative. *m*, months

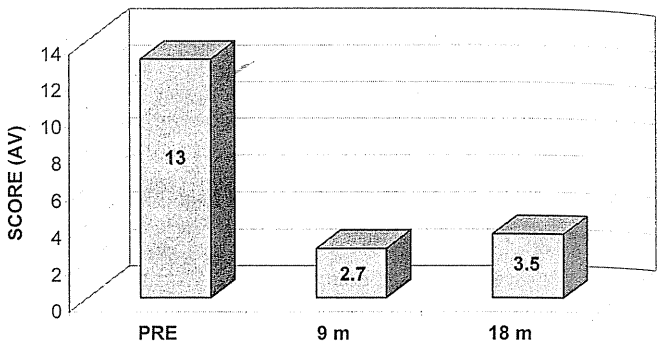

FIG. 2. IIQ results. *Av*, average. *PRE*, preoperative. *m*, months

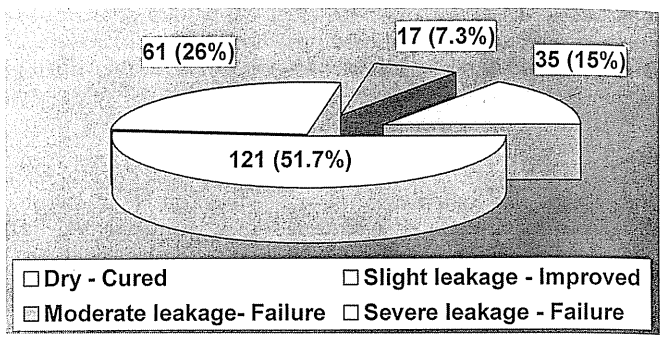

FIG. 3. UDI results. *Av*, average. *PRE*, preoperative. *m*, months

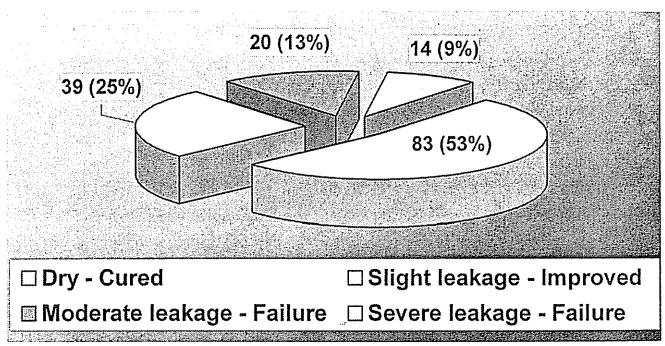

FIG. 4. Stress incontinence at 18-month followup

TABLE 3. *Type II vs III*

Type	II	III
Mos followup	21	18
IIQ score decrease (pts)	11	10.2
UDI	8.3	7.3
No. overall stress incontinence impression (%):		
Dry (cured)	64 (57)	62 (55.2)
Improved (slight leakage)	42 (37)	48 (43)
Failure (moderate + severe leakage)	6 (6)	2 (1.8)
% Improvement	83	79
Difference in No. pads daily preop to postop	2.1	2.2

Total of 112 patients.

human cryopreserved allogenic dermis from which the epidermal and dermal cellular components have been removed, leaving the basement membrane complex, which is rapidly revascularized following placement. In addition, the material is carefully screened in accordance with the American Association of Tissue Banks. Although some groups have speculated about the influence of different processing technique on the outcomes of the facia lata sling,[18] to our knowledge no prospective randomized trial have been reported and no data are available in the literature on this issue about the cadaveric dermis. Because it is acellular, it is biologically inert and less likely to induce an immune response. To our knowledge there has been no disease transmission to recipient patients to date.

We chose Repliform for use in transvaginal slings because it combines the desirable qualities of autologous and synthetic materials without the disadvantages of the increased failure rates of allograft fascia lata and the rejection or infection of synthetic materials. Repliform offers advantages over autologous tissue because of availability, ease of handling, a long shelf life and decreased donor site morbidity. Furthermore, it has limited immunogenicity and in theory it is less likely to cause inflammation and erosion than synthetic materials used for pubovaginal slings. In addition, this material offers the possibility of using a single piece of graft for concomitant pubovaginal sling placement and cystocele repair, which is the technique used in our series and described in literature.[19]

The efficacy and durability of this material has not often been reported. The few available reports of the use of freeze-dried irradiated allograft fascia sling indicate a failure rate of greater than 25%. In patients undergoing a second operation grossly degenerated allografts or a complete absence of allograft was found.[11] Therefore, it remains important to investigate the reliability and reproducibility of the material used in any sling procedure, a fact that partly prompted the current study.

We noted a 2.1% rate of intraoperative bladder perforation, which was due in all 5 cases to adherences secondary to previous transvaginally anti-incontinence procedures that made dissection difficult. We found an overall high success rate in our patients. At 18 months 78% of patients reported significant improvement in stress incontinence symptoms with 52% completely dry 100% of the time. These results were comparable for types II and III SUI. To date there have been no cases of urethral or vaginal erosion of the allograft but 4 of slow healing of the anterior vaginal wall over the Repliform graft, which resolved spontaneously within 8 weeks on conservative intravaginal antibiotic therapy. There were no cases of bone pain, osteitis pubis or osteomyelitis despite the use of bone anchors. Our high success rate at an average of 18 months of followup is comparable to that of most nonautologous sling materials and attests to the efficacy of treating hypermobility and intrinsic urethral deficiency with pubovaginal slings.

CONCLUSIONS

The use of Repliform processed human cadaveric allograft skin for the transvaginal sling procedure for SUI is effective and safe at an average intermediate followup of 18 months. Longer followup and a randomized trial comparing Repliform to other materials used in sling procedures are needed to evaluate further efficacy, durability and late complications.

APPENDIX: IIQ AND UDI

Respond to the questions below using the following scores. The score you select should reflect your PRESENT condition/situation. Please be sure to choose one number between 0 and 3.

0 = NOT AT ALL 1 = SLIGHTLY 2 = MODERATELY 3 = GREATLY

Incontinence Impact Inventory

Has urine leakage and/or prolapse affected your:

1. Ability to do household chores (cooking, laundry, housecleaning, etc.)? _____
2. Physical recreation (walking, swimming or exercise, etc.)? _____
3. Entertainment activities (movies, concerts, etc.)? _____
4. Ability to travel by car or bus more than 30 minutes from home? _____
5. Participation in social activities outside your home _____
6. Emotional health (nervousness, depression, etc.)? _____
7. Feeling frustrated? _____

Total _____

Urogenital Distress Inventory

Do you experience, and if so, how much are you bothered by:

1. Frequent urination? _____
2. Urine leakage related to the feeling of urgency? _____
3. Urine leakage related to physical activity, coughing, or sneezing, etc.? _____
4. Small amounts of urine leakage (drops)? _____
5. Difficulty emptying your bladder? _____
6. Pain of discomfort in the lower abdominal or genital area? _____

Total _____

What percentage do you think you have improved since your surgery?

Circle one: 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

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